(*c*) The batch for neomycin content, polymyxin B content, moisture, and metal particles.

(ii) Samples required:

(*a*) The neomycin sulfate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The polymyxin B sulfate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*c*) The batch:

(*1*) For all tests except sterility: A minimum of 16 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Neomycin content.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 0.1 *M* potassium phosphate buffer, pH 8.0 (solution 3), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 3. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 3. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(ii) *Polymyxin B content.* Proceed as directed in §436.105 of this chapter, except add to each concentration of the polymyxin B standard response line a quantity of neomycin to yield the same concentration of neomycin as that present when the sample is diluted to contain 10 units of polymyxin B per milliliter. Prepare the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 10 percent potassium phosphate buffer, pH 6.0 (solution 6), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 6. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 6. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of poylmyxin B per milliliter (estimated).

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(3) of that section.

(3) *Moisture.* Proceed as directed in §436.201 of this chapter.

(4) *Metal particles.* Proceed as directed in §436.206 of this chapter.

[47 FR 23442, May 28, 1982; 47 FR 25320, June 11, 1982, as amended at 50 FR 19919, May 13, 1985; 55 FR 14969, Apr. 20, 1990]

§444.380 Tobramycin ophthalmic dosage forms.

§444.380a Tobramycin ophthalmic solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Tobramycin ophthalmic solution contains in each milliliter 3.0 milligrams of tobramycin in a suitable and harmless aqueous vehicle. It contains suitable and harmless buffers, dispersants, preservatives, and tonicity agents. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of tobramycin that it is represented to contain. It is sterile. Its pH is not less than 7.0 and not more than 8.0. The tobramycin used conforms to the standards prescribed by §444.80(a)(1), except heavy metals.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The tobramycin used in making the batch for potency, moisture, pH, identity, and residue on ignition.

(*b*) The batch for potency, sterility, and pH.

(ii) Samples required:

(*a*) The tobramycin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of five immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the sample with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of tobramycin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[46 FR 16681, Mar. 13, 1981; 46 FR 22359, Apr. 17, 1981. Redesignated at 47 FR 7827, Feb. 23, 1982, and amended at 50 FR 19919, May 13, 1985; 59 FR 8399, Feb. 22, 1994]

§ 444.380b Tobramycin ophthalmic ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Tobramycin ophthalmic ointment contains, in each gram, 3.0 milligrams of tobramycin with a suitable preservative in a suitable and harmless ointment base. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of tobramycin that it is represented to contain. It is sterile. Its moisture content is not more than 1.0 percent. It passes the test for metal particles. The tobramycin used conforms to the standards prescribed by § 444.80(a)(1), except heavy metals.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The tobramycin used in making the batch for potency, moisture, pH, identity, and residue on ignition.

(*b*) The batch for potency, sterility, moisture, and metal particles.

(ii) Samples required:

(*a*) The tobramycin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 20 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of distilled water, and shake well. Allow the layers to separate. Remove the distilled water layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of distilled water. Combine the extractives in a suitable volumetric flask and dilute to volume with distilled water. Further dilute an aliquot with distilled water to the reference concentration of 2.5 micrograms of tobramycin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(3) of that section.

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *Metal particles.* Proceed as directed in § 436.206 of this chapter.

[47 FR 7827, Feb. 23, 1982; 47 FR 16320, Apr. 16, 1982, as amended at 50 FR 19919, May 13, 1985]

§ 444.380c Tobramycin-dexamethasone ophthalmic suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Tobramycin-dexamethasone ophthalmic suspension is an aqueous suspension containing, in each milliliter, 3.0 milligrams of tobramycin and